CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022407Orig1s000

CHEMISTRY REVIEW(S)

NDA 22-407

Facilities (EES) reviews

See pages 11-17 of proceeding Cycle 3 CMC Review

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

SHANNON J CREWS
07/02/2013

NDA 22-407

VIBATIV™
(telavancin)
for injection

Theravance, Inc.

Mark R. Seggel
ONDQA/DNDQA II/Branch V

for the Division of Anti-Infective Products

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Chemistry Review Data Sheet

1. NDA 22-407

2. REVIEW #: 4

3. REVIEW DATE: 29-MAY-2013

4. REVIEWER: Mark R. Seggel

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Resubmission (Class 2) [eCTD 0105] *See also DARRTS*	12-JUL-2012

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Resubmission (Class 2) [eCTD 0125]	13-MAR-2013
Amendment [eCTD 0126] (withdrawal of (b) (4))	27-MAR-2013

7. NAME & ADDRESS OF APPLICANT:

Name:	Theravance, Inc.
Address:	901 Gateway Boulevard South San Francisco, CA 94080
Representative:	Rebecca Coleman, Pharm.D.
Telephone:	650-808-6076

Reference ID: 3316551

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: VIBATIV™
b) Non-Proprietary Name (USAN): telavancin hydrochloride
c) Code Name/#: TD-6424
d) Chem. Type/Submission Priority:

- Chem. Type: 3
- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505(b)(1)

10. PHARMACOL. CATEGORY: Antibacterial

11. DOSAGE FORM: Sterile lyophilized powder for injection

12. STRENGTH/POTENCY: 250 mg per vial and 750 mg per vial

13. ROUTE OF ADMINISTRATION: Intravenous infusion

14. Rx/OTC DISPENSED: _X_Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____SPOTS product – Form Completed

__X___Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

(1) Vancomycin, $N^{3''}$-[2-(decylamino)ethyl]-29-[[(phosphonomethyl)amino]methyl]-, monohydrochloride;

(2) (3*S*,6*R*,7*R*,22*R*,23*S*,26*S*,36*R*,38a*R*)-3-(2-Amino-2-oxoethyl)-10,19-dichloro-44-[[2-*O*-[3-[[2-(decylamino)ethyl]amino]-3-*C*-methyl-2,3,6-trideoxy-α-L-*lyxo*-hexopyranosyl]-β-D-glucopyranosyl]oxy]-7,22,28,30,32-pentahydroxy-6-[[(2*R*)-4-methyl-2-(methylamino)-

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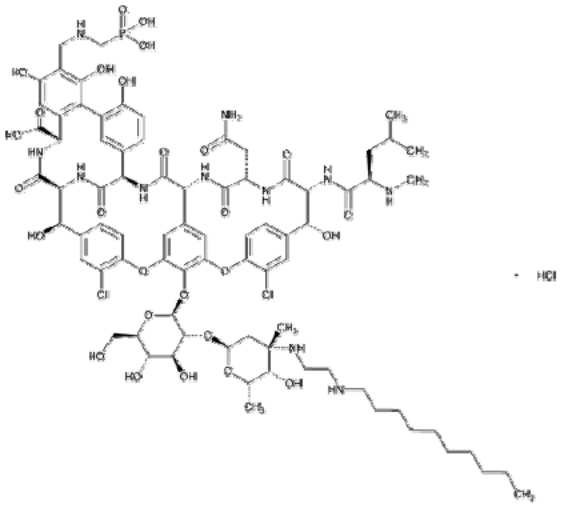
pentanoyl]amino]-2,5,24,38,39-pentaoxo-29-[[(phosphonomethyl)amino]methyl]-2,3,4,5,6,7,23,24,25,26,36,37,38,38a-tetradecahydro-8,11:18,21-dietheno-23,36-(iminomethano)-22*H*-13,16:31,35-dimetheno-1*H*,13*H*-[1,6,9]oxadiazacyclohexadecino[4,5-*m*][10,2,16]benzoxadiazacyclotetracosine-26-carboxylic acid monohydrochloride.

Molecular formula: $C_{80}H_{106}Cl_2N_{11}O_{27}P$. HCl

Molecular weight: [redacted] (b) (4) 1755.63 (free base)

CAS-560130-42-9; CAS-372151-71-8 [telavancin].



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

See NDA 22-110 and associated reviews. See also Chemistry Reviews #1 and #2 for this NDA. No changes have been reported.

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
Original application and associated reviews	NDA 22-110	Vibativ (telavancin) for injection; Approved 11-SEP-2009 for complicated skin and skin structure infections (cSSSI)
[redacted] (b) (4)		
Chemistry Review #1, 30-SEP-2009 Chemistry review #2, 03-DEC-2010	NDA 22-407 (submitted 23-JAN-2009; and first Class 2 resubmission 30-JUN-2010)	Vibativ; indicated for the treatment of nosocomial pneumonia; not approved
Chemistry Review #3, 11-JAN-2013	NDA 22-407 (second Class 2 resubmission 12-JUL-2012)	Complete Response issued 22-FEB-2013

Reference ID: 3316551

Chemistry Review #1, 29-MAY-2013	NDA 22-110/SCM-006	CMC recommendation for Approval of Hospira, McPherson, KS as new drug product manufacturer (to replace (b) (4)

18. STATUS:

ONDQA:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	na		
EES	Acceptable (see attached EES report)	06-MAY-2013	T.Gooen, Office of Compliance
Pharm/Tox	na		
Biopharm	na		
LNC	na		
Methods Validation	na		
DMEPA	na		
EA	na		
Microbiology	na		

Reference ID: 3316551

The Chemistry Review for NDA 22-407

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

NDA 22-407, which provides for a new indication (nosocomial pneumonia) for Vibativ, relies on the applicant's CMC documentation submitted to approved NDA 22-110. NDA 22-407 was issued a Complete Response letter on 22-Feb-2013 due to cGMP deficiencies at [redacted] (b) (4), the drug product manufacturing facility. The [redacted] (b) (4) facility has now been withdrawn from the NDA and a new drug product manufacturing facility, Hospira McPherson, Kansas has been recommended for approval (see NDA 22110/S-006 Chemistry Review #1, 29-MAY-2013).

The Office of Compliance has issued an Overall Recommendation of Acceptable for NDA 22-407 (see attached EES report).

The package insert for Vibativ approved under NDA 22-110 has been updated to reflect the additional clinical indication and to update safety information. Other minor changes to the labeling (package insert, vial label and carton) are acceptable from the chemistry, manufacturing, and controls perspective.

Overall, NDA 22-407 is recommended for approval from the chemistry, manufacturing and controls perspective.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

Not Applicable

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

See NDA 22-110 and associated chemistry reviews as well as previous chemistry reviews for NDA 22-407.

B. Description of How the Drug Product is Intended to be Used

Reference ID: 3316551

Vibativ (telavancin) for injection is approved for the treatment of complicated skin and skin structure infections (cSSSI) under NDA 22-110. The proposed indication covers use of Vibativ for the treatment of nosocomial pneumonia (HABP/VABP).

The product is labeled for storage at 2-8°C [redacted] (b) (4). The current expiration dating period is [redacted] (b) (4).

C. Basis for Approvability or Not-Approval Recommendation

NDA 22-407, which provides for a new indication (nosocomial pneumonia) for Vibativ (telavancin) for injection, relies on the applicant's CMC documentation submitted to approved NDA 22-110.

NDA 22-407 was issued a Complete Response letter on 22-FEB-2013, "because it [did] not meet the standards for approval under Section 505 of the Federal Food Drug & Cosmetic Act (FD&C Act). Specifically, as provided in 505(d), the Agency will refuse to approve the application if "the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to preserve its identity, strength, quality, and purity" of the product. See 21 CFR 314.110(a); 314.125(b)(1)." The Complete Response letter referred to the significant cGMP issues at [redacted] (b) (4).

Problems at [redacted] (b) (4) included [redacted] (b) (4). Telavancin for injection was voluntarily withdrawn from distribution in November 2011. On January 31, 2013, the United States District Court [redacted] (b) (4) approved a Consent Decree of Permanent Injunction against [redacted] (b) (4). This decree precludes [redacted] (b) (4) from, among other things, manufacturing, processing, packing, labeling, holding, or distributing non-medically necessary drugs until a remediation plan has been implemented and numerous conditions are met.

In light of the cGMP issues at [redacted] (b) (4), Theravance identified and qualified a new drug product manufacturer, Hospira McPherson located in McPherson, Kansas. This new drug product manufacturing facility has been recommended for approval as a replacement for the problematic [redacted] (b) (4) facility (see NDA 22-110/S-006 Chemistry Review #1, 29-MAY-2013). [redacted] (b) (4) has been withdrawn as a drug product manufacturing facility (see the 27-MAR-2013 submission to NDA 22-407).

All facilities involved in the manufacture, packaging and control of Vibativ, including Hospira, have acceptable cGMP status. The Office of Compliance issued an Overall Recommendation of Acceptable for NDA 22-407 on 06-MAY-2013 (see attached EES report).

The package insert for Vibativ first approved under NDA 22-110 has been updated to reflect the additional clinical indication and to update safety information. The Description and How Supplied sections of the package insert are unaffected by addition of the new indication, although the NDCs have been revised to reflect a change in

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formal product ownership. Only minor changes to reflect changes in product ownership and NDC have been made to the vial label and carton. Based on recommendations from DMEPA, minor changes to the Preparation and Administration section have been made in order to minimize foaming that may occur during reconstitution; this should reduce the potential for dosing errors. Overall, the updated labeling is acceptable from the chemistry, manufacturing, and controls perspective.

III. Administrative

A. Reviewer's Signature

{see electronic signature page}
Mark R. Seggel, Chemist

B. Endorsement Block

{see electronic signature page}
Rapti Madurawe, Ph.D., Branch Chief

C. CC Block

{see darrts}

Chemistry Assessment

I. Review Of Common Technical Document-Quality (Ctd-Q) Module 3.2: Body Of Data

S DRUG SUBSTANCE

See NDA 22-110 and associated reviews.

P DRUG PRODUCT

See NDA 22-110 and associated reviews.

A APPENDICES

See NDA 22-110 and associated reviews.

R REGIONAL INFORMATION

See NDA 22-110 and associated reviews.

II. Review Of Common Technical Document-Quality (Ctd-Q) Module 1

A. Labeling & Package Insert

Comments: The package insert has been revised to incorporate the proposed nosocomial pneumonia indication and supporting data. Other changes to the labeling (package insert, container and carton labels) have been made that reflect that Astellas is no longer involved in the marketing and distribution of Vibativ.

The revised labeling indicates that Vibativ is now a registered trademark of Theravance, Inc.; formerly the trademark was held by Astellas. The NDC numbers listed in the package insert have been changed to reflect that Astellas is no longer involved in the marketing and distribution of Vibativ.

B. Environmental Assessment Or Claim Of Categorical Exclusion

"In accordance with 21 CFR 25.31(b), Theravance, Inc., requests a categorical exclusion for an environmental assessment for Telavancin for Injection on the basis that the estimated concentrations of Telavancin at the point-of-entry into the aquatic environment will be below

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1 part per billion. Theravance, Inc. does not have any knowledge of any extraordinary circumstances that that would warrant the preparation of an environmental assessment."

Comments: The categorical exclusion from the preparation of an environmental assessment (EA) is acceptable based the applicant's analysis and determination of an EIC less than 1 ppb.

III. List Of Deficiencies To Be Communicated

Not Applicable

Attachment 1. EES Report

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT

Application:	NDA 22407/000	**Action Goal:**	
Stamp Date:	26-JAN-2009	**District Goal:**	15-JUL-2013
Regulatory:	13-SEP-2013		
Applicant:	THERAVANCE INC	**Brand Name:**	VIBATIV
	901 GATEWAY BLVD	**Estab. Name:**	
	SOUTH SAN FRANCISCO, CA 94080	**Generic Name:**	
Priority:		**Product Number; Dosage Form; Ingredient; Strengths**	
Org. Code:	520	001; POWDER, FOR INJECTION SOLUTION, LYOPHILIZED; TELAVANCIN HYDROCHLORIDE; 250MG 002; POWDER, FOR INJECTION SOLUTION, LYOPHILIZED; TELAVANCIN HYDROCHLORIDE; 750MG	

Application Comment: NEW MOLECULAR ENTITY. DRUG SUBSTANCE, DRUG PRODUCT, AND ESTABLISHMENTS ARE THE SAME AS NDA 22-110. NDA 22-110 RECEIVED OVERALL RECOMMENDATION OF ACCEPTABLE ON 04-JUN-2008 (FORMERLY WITHHOLD ON 13-AUG-2007 AND 03-JUL-2007). (on 23-MAR-2009 by J. DAVID () 3017964247)

CLASS 2 RESUBMISSION (6-MO CLOCK): PDUFA IS JUNE 22, 2010. (on 23-DEC-2009 by J. DAVID () 3017964247)

FDA Contacts:	B. SHANMUGAM	Prod Qual Reviewer		3017961457
	K. SNOW	Micro Reviewer	(HFD-520)	3017960736
	A. CUFF	Product Quality PM	(HF-01)	3017964061
	J. DAVI	Regulatory Project Mgr	(HFD-520)	3017960702
	R. MADURAWE	Team Leader		3017961408

Overall Recommendation:	ACCEPTABLE	on 06-MAY-2013	by T. GOOEN	(HFD-320)	3017963257
	WITHHOLD	on 09-JAN-2013	by T. GOOEN	(HFD-320)	3017963257
	WITHHOLD	on 05-JUL-2011	by EES_PROD		
	ACCEPTABLE	on 10-FEB-2010	by EES_PROD		
	ACCEPTABLE	on 22-JUN-2009	by EES_PROD		

Chemistry Assessment Section

Establishment: **CFN:** (b) (4) **FEI:** (b) (4)

(b) (4)

DMF No: **AADA:** N 022110

Responsibilities: FINISHED DOSAGE STABILITY TESTER

Establishment Comment: DRUG SUBSTANCE STABILITY TESTING; DRUG PRODUCT STABILITY TESTING. (on 23-MAR-2009 by J. DAVID () 3017964247)

Profile: CONTROL TESTING LABORATORY **OAI Status:** NONE

Milestone Name	Milestone Date	Request Type	Planned Completion	Decision	Creator
Comment				Reason	
SUBMITTED TO OC	23-MAR-2009				DAVIDJE
SUBMITTED TO DO	23-MAR-2009	10-Day Letter			FERGUSONS
DO RECOMMENDATION	01-APR-2009			ACCEPTABLE	MFADDEN
A GENERAL CGMP INSPECTION WAS CONDUCTED AT THIS FACILITY ON (b) (4) COVERING THE LABORATORY AND QUALITY SYSTEMS. THAT INSPECTION DID NOT RESULT IN THE ISSUANCE OF A FD 483. FOUR VERBAL OBSERVATIONS WERE DISCUSSED WITH THE FIRM. THE VERBAL OBSERVATIONS WERE REGARDING LACK OF A CAPA FOR A UV SPECTROMETER WITH A SOFTWARE PROBLEM, CHEMICAL/REGAGENTS WERE OBSERVED TO NOT BE LABELED CORRECTLY, EXPIRED PURIFIED WATER WAS USED IN AN ANALYSIS AND IT WAS NOT NOTED BY THE REVIEWERS, AND PRE-NUMBERED WORKSHEETS ARE NOT CONTROLLED AS WELL AS THEY SHOULD BE. MANAGEMENT HAD IMPLEMENTED OR PROMISED CORRECTIVE ACTION PRIOR TO THE CLOSE OF THE INSPECTION FOR THESE ITEMS. BASED UPON THIS INSPECTION AND THE FIRM'S COMPLIANCE HISTORY, (b) (4) RECOMMENDS THEM AS ACCEPTABLE.				INSPECTION	
OC RECOMMENDATION	01-APR-2009			ACCEPTABLE	STOCKM
				DISTRICT RECOMMENDATION	
SUBMITTED TO OC	23-DEC-2009				DAVIDJE
SUBMITTED TO DO	24-DEC-2009	Product Specific			INYARDA
DO RECOMMENDATION	06-JAN-2010			ACCEPTABLE	MFADDEN
AN INSPECTION WAS CONDUCTED AT THIS FACILITY ON (b) (4) COVERING CGMP'S AND THIS FIRM'S ABILITY TO CONDUCT FINISHED PRODUCT AND STABILITY TESTING UNDER CONTRACT FOR VARIOUS CLIENTS. THIS INSPECTION DID NOT RESULT IN THE ISSUANCE OF A FD 483. FOUR VERBAL OBSERVATIONS WERE DISCUSSED REGARDING CGMP ISSUES. MANAGEMENT INITIATED CORRECTIVE ACTION TO THESE OBSERVATIONS PRIOR TO THE CLOSE OF THE INSPECTION. BASED UPON THIS INSPECTION AND THE FIRM'S INSPECTION HISTORY, (b) (4) RECOMMENDS THEM AS ACCEPTABLE.				BASED ON FILE REVIEW	
OC RECOMMENDATION	06-JAN-2010			ACCEPTABLE	INYARDA
				DISTRICT RECOMMENDATION	
SUBMITTED TO OC	30-JUL-2012				CUFFA
OC RECOMMENDATION	30-JUL-2012			ACCEPTABLE	SAFAAIJAZIR
				BASED ON PROFILE	
SUBMITTED TO OC	04-APR-2013				CUFFA
SUBMITTED TO OC	04-APR-2013				CUFFA
SUBMITTED TO DO	05-APR-2013	Product Specific			SHARPT
THIS IS A NME. AS PER FACTS, THIS PARTICULAR NDA WAS NOT COVERED DURING THE					

Reference ID: 3316551

Chemistry Assessment Section

LAST INSPECTION IN (b) (4)

DO RECOMMENDATION 05-APR-2013 ACCEPTABLE MFADDEN

A CGMP INSPECTION WAS CONDUCTED (b) (4) FOCUSING ON THE CONTROL TESTING LABORATORY. NO FDA 483 WAS ISSUED. SEVERAL VERBAL OBSERVATIONS WERE DISCUSSED AND CORRECTED DURING THE COURSE OF THE INSPECTION. BASED UPON THE FIRM'S HISTORY AND THIS LAST INSPECTION, (b) (4) RECOMMENDS THIS FIRM AS ACCEPTABLE.

BASED ON FILE REVIEW

OC RECOMMENDATION 05-APR-2013 ACCEPTABLE SHARPT

DISTRICT RECOMMENDATION

Establishment: **CFN:** 1925262 **FEI:** 1925262

HOSPIRA WORLDWIDE, INC

1776 CENTENNIAL DR
MCPHERSON, KS 674609301

DMF No: **AADA:**

Responsibilities: FINISHED DOSAGE MANUFACTURER

Establishment Comment: DRUG PRODUCT MANUFACTURER (on 04-APR-2013 by A. CUFF (HF-01) 3017964061)

Profile: SMALL VOLUME PARENTERAL, LYOPHILIZED **OAI Status:** NONE

Milestone Name	Milestone Date	Request Type	Planned Completion	Decision	Creator
Comment				Reason	
SUBMITTED TO OC	04-APR-2013				CUFFA
SUBMITTED TO DO	05-APR-2013	Product Specific			SHARPT
THIS IS A NME. AS PER FACTS, THIS PARTICULAR NDA WAS NOT COVERED DURING THE LAST INSPECTION IN (b) (4)					
ASSIGNED INSPECTION TO IB	24-APR-2013	Product Specific			SBERRYMA
SUBMITTED TO DO	06-MAY-2013	10-Day Letter			SHARPT
THE SUBJECT APPLICATION APPEARS TO BE ERRONEOUSLY FLAGGED AS AN NME IN DARRTS.BECAUSE OF THIS ERROR, EES LOOKS LIKE THE ASSOCIATED HOSPIRA SITE IS MANUFACTURING AN NME (FLAGGED IN BABY BLUE). HOWEVER, IT¿S THE SAME PRODUCT AS FOR 22110/006 (WHICH WAS GIVEN AN ACCEPTABLE RECOMMENDATION FOR IN APRIL 2013). RESUBMITTING TO DISTRICT FOR RECOMMENDATION.					
DO RECOMMENDATION	06-MAY-2013			ACCEPTABLE	SBERRYMA
THE LAST EIR OF 10/9-10/24/12 WAS CLASSIFIED VAI & FOUND SVL PROFILE CLASS ACCEPTABLE. FARS AND DQRS RECEIVED SINCE THE PREVIOUS INSPECTION DO NOT INDICATE A REASON FOR WITHHOLD. BASED ON FILE REVIEW, KAN-DO RECOMMENDS APPROVABLE FOR THIS APPLICATION.				BASED ON FILE REVIEW	
OC RECOMMENDATION	06-MAY-2013			ACCEPTABLE	TGOOEN
APPLICATION ORIGINALLY FLAGGED AS AN NME THROUGH MANUAL CHECK OF PRODUCT "NME" CHECKBOX TRIGGER. THIS IS NOT AN NME.				DISTRICT RECOMMENDATION	

Reference ID: 3316551

Chemistry Assessment Section

Establishment: **CFN:** (b) (4) **FEI:** (b) (4)

(b) (4)

DMF No: **AADA:** N 022110

Responsibilities: FINISHED DOSAGE STABILITY TESTER

Establishment Comment: MICROBIOLOGICAL TESTING OF STABILITY SAMPLES. (on 23-MAR-2009 by J. DAVID () 3017964247)

Profile: CONTROL TESTING LABORATORY **OAI Status:** NONE

Milestone Name	Milestone Date	Request Type	Planned Completion	Decision	Creator
Comment				Reason	
SUBMITTED TO OC	23-MAR-2009				DAVIDJE
OC RECOMMENDATION	23-MAR-2009			ACCEPTABLE BASED ON PROFILE	FERGUSONS
SUBMITTED TO OC	23-DEC-2009				DAVIDJE
SUBMITTED TO DO	24-DEC-2009	Product Specific			INYARDA
ASSIGNED INSPECTION TO IB	29-DEC-2009	Product Specific			ESMITH1
INSPECTION SCHEDULED	29-DEC-2009		(b) (4)		ESMITH1
INSPECTION PERFORMED	(b) (4)				MATTHEW.DIONNE
See Endorsement Text.					
INSPECTION PERFORMED	(b) (4)				ESMITH1
DO RECOMMENDATION	27-JAN-2010			ACCEPTABLE INSPECTION	ESMITH1
OC RECOMMENDATION	28-JAN-2010			ACCEPTABLE DISTRICT RECOMMENDATION	INYARDA
SUBMITTED TO OC	30-JUL-2012				CUFFA
SUBMITTED TO DO	30-JUL-2012	10-Day Letter			SAFAAIJAZIR
DO RECOMMENDATION	01-AUG-2012			ACCEPTABLE BASED ON FILE REVIEW	CLE
PREVIOUS THREE EI DRUG INSPECTIONS (2012, 2010, AND 2008) WERE CLASSIFIED VAI AND NAI FOR PROFILE CLASS CTL. DISTRICT RECOMMENDS APPROVAL BASED ON COMPLIANCE HISTORY OF THE FIRM.					
OC RECOMMENDATION	02-AUG-2012			ACCEPTABLE DISTRICT RECOMMENDATION	INYARDA
SUBMITTED TO OC	04-APR-2013				CUFFA
SUBMITTED TO OC	04-APR-2013				CUFFA
SUBMITTED TO DO	05-APR-2013	10-Day Letter			SHARPT
CTL INITIAL. THIS IS A NME, BUT THIS IS FOR MICRO TESTING					

Reference ID: 3316551

Chemistry Assessment Section

DO RECOMMENDATION	18-APR-2013	ACCEPTABLE	EBUTLER
PROFILE CLASS CTX FOUND ACCEPTABLE. PREVIOUS THREE INSPECTIONS WERE VAI, NAI, NAI (2012,2010,2008). RECOMMEND APPROVAL BASED ON FIRM'S COMPLIANCE HISTORY.		BASED ON FILE REVIEW	
OC RECOMMENDATION	18-APR-2013	ACCEPTABLE	PRABHAKARAR
PROFILE CLASS CTX FOUND ACCEPTABLE. PREVIOUS THREE INSPECTIONS WERE VAI, NAI, NAI (2012,2010,2008). RECOMMEND APPROVAL BASED ON FIRM'S COMPLIANCE HISTORY.		DISTRICT RECOMMENDATION	

Reference ID: 3316551

Chemistry Assessment Section

Establishment: **CFN:** (b) (4) **FEI:** (b) (4)
(b) (4)

DMF No: **AADA:** N 022110

Responsibilities: DRUG SUBSTANCE MANUFACTURER

Establishment Comment: DRUG SUBSTANCE IS AN NME. THIS FACILITY IS RESPONSIBLE FOR MANUFACTURING AND RELEASE TESTING. (on 23-MAR-2009 by J. DAVID () 3017964247)

Profile: (b) (4) **OAI Status:** NONE

Milestone Name / Comment	Milestone Date	Request Type	Planned Completion	Decision / Reason	Creator
SUBMITTED TO OC	23-MAR-2009				DAVIDJE
SUBMITTED TO DO	23-MAR-2009	Product Specific			STOCKM
DO RECOMMENDATION	06-APR-2009			ACCEPTABLE BASED ON FILE REVIEW	JOHNSONE
OC RECOMMENDATION	06-APR-2009			ACCEPTABLE DISTRICT RECOMMENDATION	STOCKM
SUBMITTED TO OC	23-DEC-2009				DAVIDJE
SUBMITTED TO DO	24-DEC-2009	Product Specific			INYARDA
DO RECOMMENDATION	19-JAN-2010			ACCEPTABLE BASED ON FILE REVIEW	JOHNSONE
OC RECOMMENDATION	19-JAN-2010			ACCEPTABLE DISTRICT RECOMMENDATION	STOCKM
SUBMITTED TO OC	30-JUL-2012				CUFFA
SUBMITTED TO DO	30-JUL-2012	10-Day Letter			SAFAAIJAZIR
UNDER REVIEW	31-JUL-2012				PHILPYE
DO RECOMMENDATION INSPECTION ENDING (b) (4) CLASSIFIED VAI.	27-AUG-2012			ACCEPTABLE BASED ON FILE REVIEW	STOCKM
OC RECOMMENDATION	31-AUG-2012			ACCEPTABLE DISTRICT RECOMMENDATION	SAFAAIJAZIR
SUBMITTED TO OC	04-APR-2013				CUFFA
SUBMITTED TO OC	04-APR-2013				CUFFA
SUBMITTED TO DO THIS IS A NME. AS PER FACTS, THIS PARTICULAR NDA WAS NOT COVERED DURING THE LAST INSPECTION IN OCT 2012	05-APR-2013	Product Specific			SHARPT
DO RECOMMENDATION SITE INSPECTED (b) (4) AND COVERED TELAVANCIN. THIS IS NOT AN NME, BECAUSE SISTER NDA#22110 WAS APPROVED AND TRIGGERED SURVEILLANCE COVERAGE ON 2012	16-APR-2013			ACCEPTABLE INSPECTION	TUNGL

Reference ID: 3316551

INSPECTION.

OC RECOMMENDATION	16-APR-2013	ACCEPTABLE	PRABHAKARAR
SITE INSPECTED (b) (4) AND COVERED TELAVANCIN. THIS IS NOT AN NME, BECAUSE SISTER NDA#22110 WAS APPROVED AND TRIGGERED SURVEILLANCE COVERAGE ON 2012 INSPECTION.		DISTRICT RECOMMENDATION	

####

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

MARK R SEGGEL
05/30/2013

RAPTI D MADURAWE
05/31/2013

NDA 22-407

VIBATIV™
(telavancin)
for injection

Theravance, Inc.

Mark R. Seggel
ONDQA/DNDQA II/Branch V

for the Division of Anti-Infective Products

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A. Recommendation and Conclusion on Approvability 7

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable 7

II. Summary of Chemistry Assessments 7

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Chemistry Review Data Sheet

1. NDA 22-407

2. REVIEW #: 3

3. REVIEW DATE: 11-JAN-2013

4. REVIEWER: Mark R. Seggel

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
see DARRTS	

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Resubmission (Class 2) [eCTD 0105]	12-JUL-2012

7. NAME & ADDRESS OF APPLICANT:

Name:	Theravance, Inc.
Address:	901 Gateway Boulevard South San Francisco, CA 94080
Representative:	Rebecca Coleman, Pharm.D.
Telephone:	650-808-6076

8. DRUG PRODUCT NAME/CODE/TYPE:

Reference ID: 3244056

a) Proprietary Name: VIBATIV™
b) Non-Proprietary Name (USAN): telavancin hydrochloride
c) Code Name/#: TD-6424
d) Chem. Type/Submission Priority:

- Chem. Type: 3
- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505(b)(1)

10. PHARMACOL. CATEGORY: Antibacterial

11. DOSAGE FORM: Sterile lyophilized powder for injection

12. STRENGTH/POTENCY: 250 mg per vial and 750 mg per vial

13. ROUTE OF ADMINISTRATION: Intravenous infusion

14. Rx/OTC DISPENSED: _X_Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____SPOTS product – Form Completed

__X___Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

(1) Vancomycin, $N^{3''}$-[2-(decylamino)ethyl]-29-[[(phosphonomethyl)amino]methyl]-, monohydrochloride;

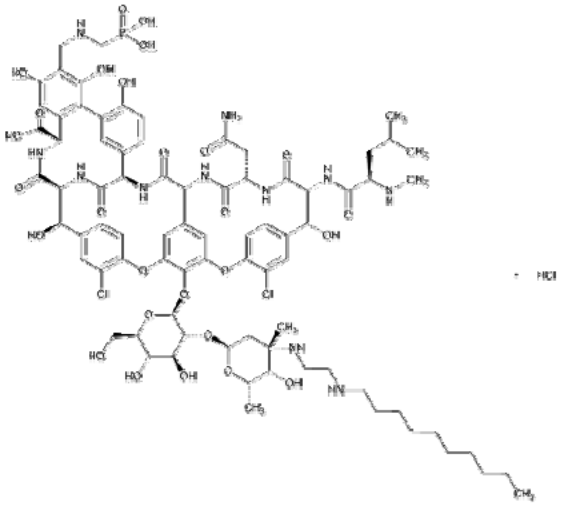
(2) (3*S*,6*R*,7*R*,22*R*,23*S*,26*S*,36*R*,38a*R*)-3-(2-Amino-2-oxoethyl)-10,19-dichloro-44-[[2-*O*-[3-[[2-(decylamino)ethyl]amino]-3-*C*-methyl-2,3,6-trideoxy-α-L-*lyxo*-hexopyranosyl]-β-D-glucopyranosyl]oxy]-7,22,28,30,32-pentahydroxy-6-[[(2*R*)-4-methyl-2-(methylamino)-pentanoyl]amino]-2,5,24,38,39-pentaoxo-29-[[(phosphonomethyl)amino]methyl]-2,3,4,5,6,7,23,24,25,26,36,37,38,38a-tetradecahydro-8,11:18,21-dietheno-23,36-

(iminomethano)-22*H*-13,16:31,35-dimetheno-1*H*,13*H*-[1,6,9]oxadiazacyclohexadecino[4,5-*m*][10,2,16]benzoxadiazacyclotetracosine-26-carboxylic acid monohydrochloride.

Molecular formula: $C_{80}H_{106}Cl_2N_{11}O_{27}P$. HCl

Molecular weight: (b) (4) 1755.63 (free base)

CAS-560130-42-9; CAS-372151-71-8 [telavancin].



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

See NDA 22-110 and associated reviews. See also Chemistry Reviews #1 and #2 for this NDA. No changes have been reported.

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
Original application and associated reviews	NDA 22-110	Vibativ (telavancin) for injection; Approved 11-SEP-2009 for complicated skin and skin structure infections (cSSSI)
		(b) (4)
Chemistry Review #1, 30-SEP-2009 Chemistry review #2, 03-DEC-2010	NDA 22-407 (submitted 23-JAN-2009, and first resubmission (submitted 30-JUN-2010)	Vibativ; indicated for the treatment of nosocomial pneumonia; not approved

Reference ID: 3244056

18. STATUS:

ONDC:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	na		
EES	Withhold (see attached EES report)	09-JAN-2012	T.Gooen, Office of Compliance
Pharm/Tox	na		
Biopharm	na		
LNC	na		
Methods Validation	na		
DMEPA	na		
EA	na		
Microbiology	na		

The Chemistry Review for NDA 22-407

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

NDA 22-407, which provides for a new indication (nosocomial pneumonia) for Vibativ, relies on the applicant's CMC documentation submitted to approved NDA 22-110. However, at this time NDA 22-407 is not recommended for approval due to an overall recommendation of Withhold issued by the Office of Compliance on 09-JAN-2013. This recommendation is based on the significant cGMP issues identified at the drug product manufacturing site, [redacted] (b) (4) (see attached EES report).

Labeling negotiations have not been completed at this time; labeling will be finalized [redacted] (b) (4)

From the chemistry, manufacturing and controls perspective NDA 22-407 is not recommended for approval.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

Not Applicable

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

See NDA 22-110 and associated chemistry reviews as well as previous chemistry reviews for NDA 22-407.

B. Description of How the Drug Product is Intended to be Used

Vibativ (telavancin) for injection is approved for the treatment of complicated skin and skin structure infections (cSSSI) under NDA 22-110. The proposed indication covers use of Vibativ for the treatment of nosocomial pneumonia (HABP/VABP).

The product is labeled for storage at 2-8°C [redacted] (b) (4) The current expiration dating period is [redacted] (b) (4)

Reference ID: 3244056

C. Basis for Approvability or Not-Approval Recommendation

Significant cGMP issues have been identified at [redacted] (b) (4) affecting a range of sterile intravenous products. Problems include [redacted] (b) (4). Telavancin for injection was [voluntarily] withdrawn from distribution in November 2011.

The Office of Compliance issued an overall recommendation of Withhold for this application on 09-JAN-2013 (see attached EES report). Therefore this application cannot be approved from the CMC perspective.

III. Administrative

A. Reviewer's Signature

{see electronic signature page}

Mark R. Seggel, Chemist

B. Endorsement Block

{see electronic signature page}

Rapti Madurawe, Ph.D., Branch Chief

C. CC Block

{see darrts}

Chemistry Assessment

I. Review Of Common Technical Document-Quality (Ctd-Q) Module 3.2: Body Of Data

S DRUG SUBSTANCE

See NDA 22-110 and associated reviews.

P DRUG PRODUCT

See NDA 22-110 and associated reviews.

A APPENDICES

See NDA 22-110 and associated reviews.

R REGIONAL INFORMATION

See NDA 22-110 and associated reviews.

II. Review Of Common Technical Document-Quality (Ctd-Q) Module 1

A. Labeling & Package Insert

Comments: The package insert has been revised to incorporate the proposed nosocomial pneumonia indication and supporting data. Other changes to the labeling (package insert, container and carton labels) have been made that reflect that Astellas is no longer involved in the marketing and distribution of Vibativ. Labeling negotiations will be completed under NDA 22-110 (b) (4)

The revised labeling indicates that Vibativ is a registered trademark of Theravance, Inc. However, this is not currently reflected in the uspto.gov database, which indicates that the trademark is still registered to Astellas.

The NDC numbers listed in the package insert have been changed, presumably to reflect that Astellas is no longer involved in the marketing and distribution of Vibativ. However, the FDA's NDC directory only links Vibativ with the previous Astellas NDC numbers.

Reference ID: 3244056

B. Environmental Assessment Or Claim Of Categorical Exclusion

"In accordance with 21 CFR 25.31(b), Theravance, Inc., requests a categorical exclusion for an environmental assessment for Telavancin for Injection on the basis that the estimated concentrations of Telavancin at the point-of-entry into the aquatic environment will be below 1 part per billion. Theravance, Inc. does not have any knowledge of any extraordinary circumstances that that would warrant the preparation of an environmental assessment."

Comments: The categorical exclusion from the preparation of an environmental assessment (EA) is acceptable based the applicant's analysis and determination of an EIC less than 1 ppb.

III. List Of Deficiencies To Be Communicated

Not Applicable

Attachment 1. EES Report

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT

Application:	NDA 22407/000	**Action Goal:**	
Stamp Date:	26-JAN-2009	**District Goal:**	13-NOV-2012
Regulatory:	12-JAN-2013		
Applicant:	THERAVANCE INC 901 GATEWAY BLVD SOUTH SAN FRANCISCO, CA 94080	**Brand Name:** **Estab. Name:** **Generic Name:**	VIBATIV
Priority:		**Product Number; Dosage Form; Ingredient; Strengths**	
Org. Code:	520	001; POWDER, FOR INJECTION SOLUTION, LYOPHILIZED; TELAVANCIN HYDROCHLORIDE; 250MG 002; POWDER, FOR INJECTION SOLUTION, LYOPHILIZED; TELAVANCIN HYDROCHLORIDE; 750MG	

Application Comment: NEW MOLECULAR ENTITY. DRUG SUBSTANCE, DRUG PRODUCT, AND ESTABLISHMENTS ARE THE SAME AS NDA 22-110. NDA 22-110 RECEIVED OVERALL RECOMMENDATION OF ACCEPTABLE ON 04-JUN-2008 (FORMERLY WITHHOLD ON 13-AUG-2007 AND 03-JUL-2007). (on 23-MAR-2009 by J. DAVID () 3017964247)

CLASS 2 RESUBMISSION (6-MO CLOCK): PDUFA IS JUNE 22, 2010. (on 23-DEC-2009 by J. DAVID () 3017964247)

FDA Contacts:				
	A. CUFF	Project Manager	(HF-01)	3017964061
	B. SHANMUGAM	Review Chemist		3017961457
	R. MADURAWE	Team Leader		3017961408

Overall Recommendation:					
	WITHHOLD	on 09-JAN-2013	by T. GOOEN	(HFD-320)	3017963257
	WITHHOLD	on 05-JUL-2011	by EES_PROD		
	ACCEPTABLE	on 10-FEB-2010	by EES_PROD		
	ACCEPTABLE	on 22-JUN-2009	by EES_PROD		

Establishment: **CFN:** (b) (4) (b) (4) **FEI:** (b) (4)

DMF No: **AADA:** N 022110

Responsibilities: FINISHED DOSAGE MANUFACTURER

Establishment Comment: DRUG PRODUCT MANUFACTURING, RELEASE TESTING, PACKAGING AND LABELING. DMF (b) (4) IS REFERENCED FOR (b) (4) AT THIS FACILITY. (on 23-MAR-2009 by J. DAVID () 3017964247)

Profile: SMALL VOLUME PARENTERAL, LYOPHILIZED **OAI Status:** POTENTIAL OAI

Milestone Name / Comment	Milestone Date	Request Type	Planned Completion	Decision / Reason	Creator
SUBMITTED TO OC	23-MAR-2009				DAVIDJE
SUBMITTED TO DO	23-MAR-2009	Product Specific			FERGUSONS
DO RECOMMENDATION PAI ENDING (b) (4) FOR SIMILAR NDA 22-110 DID NOT IDENTIFY SPECIFIC PROBLEMS RELATED TO 22-110 PRODUCT. GMP PROFILES ARE CURRENTLY ACCEPTABLE BASED ON COMPREHENSIVE GMP INSPECTION CONDUCTED (b) (4) WHICH WAS VAI.	22-JUN-2009			ACCEPTABLE BASED ON FILE REVIEW	KCULVER
OC RECOMMENDATION	22-JUN-2009			ACCEPTABLE DISTRICT RECOMMENDATION	FERGUSONS
SUBMITTED TO OC	23-DEC-2009				DAVIDJE
SUBMITTED TO DO	24-DEC-2009	Product Specific			INYARDA
DO RECOMMENDATION NO REASON TO CHANGE PREVIOUS DO RECOMMENDATION; SVL PROFILEIS ACCEPTABLE.	10-FEB-2010			ACCEPTABLE BASED ON FILE REVIEW	KCULVER
OC RECOMMENDATION	10-FEB-2010			ACCEPTABLE DISTRICT RECOMMENDATION	CRUZC
SUBMITTED TO OC	30-JUL-2012				CUFFA
SUBMITTED TO DO	30-JUL-2012	10-Day Letter			SAFAAIJAZIR
DO RECOMMENDATION CONSENT DECREE NEGOTIATIONS ONGOING WITH FIRM.	18-SEP-2012			WITHHOLD PENDING REGULATORY ACTION WITH	KCULVER
OC RECOMMENDATION CD SIGNING IN PROCESS	09-JAN-2013			WITHHOLD WARNING LETTER ISSUED	TGOOEN

Chemistry Assessment Section

Establishment: **CFN:** (b) (4) (b) (4) **FEI:** (b) (4)

DMF No: **AADA:** N 022110

Responsibilities: FINISHED DOSAGE STABILITY TESTER

Establishment Comment: DRUG SUBSTANCE STABILITY TESTING; DRUG PRODUCT STABILITY TESTING. (on 23-MAR-2009 by J. DAVID () 3017964247)

Profile: CONTROL TESTING LABORATORY **OAI Status:** NONE

Milestone Name / Comment	Milestone Date	Request Type	Planned Completion	Decision / Reason	Creator
SUBMITTED TO OC	23-MAR-2009				DAVIDJE
SUBMITTED TO DO	23-MAR-2009	10-Day Letter			FERGUSONS
DO RECOMMENDATION	01-APR-2009			ACCEPTABLE	MFADDEN
A GENERAL CGMP INSPECTION WAS CONDUCTED AT THIS FACILITY ON (b) (4) COVERING THE LABORATORY AND QUALITY SYSTEMS. THAT INSPECTION DID NOT RESULT IN THE ISSUANCE OF A FD 483. FOUR VERBAL OBSERVATIONS WERE DISCUSSED WITH THE FIRM. THE VERBAL OBSERVATIONS WERE REGARDING LACK OF A CAPA FOR A UV SPECTROMETER WITH A SOFTWARE PROBLEM, CHEMICAL/REGAGENTS WERE OBSERVED TO NOT BE LABELED CORRECTLY, EXPIRED PURIFIED WATER WAS USED IN AN ANALYSIS AND IT WAS NOT NOTED BY THE REVIEWERS, AND PRE-NUMBERED WORKSHEETS ARE NOT CONTROLLED AS WELL AS THEY SHOULD BE. MANAGEMENT HAD IMPLEMENTED OR PROMISED CORRECTIVE ACTION PRIOR TO THE CLOSE OF THE INSPECTION FOR THESE ITEMS. BASED UPON THIS INSPECTION AND THE FIRM'S COMPLIANCE HISTORY, MIN-DO RECOMMENDS THEM AS ACCEPTABLE.				INSPECTION	
OC RECOMMENDATION	01-APR-2009			ACCEPTABLE DISTRICT RECOMMENDATION	STOCKM
SUBMITTED TO OC	23-DEC-2009				DAVIDJE
SUBMITTED TO DO	24-DEC-2009	Product Specific			INYARDA
DO RECOMMENDATION	06-JAN-2010			ACCEPTABLE	MFADDEN
AN INSPECTION WAS CONDUCTED AT THIS FACILITY ON (b) (4) COVERING CGMP'S AND THIS FIRM'S ABILITY TO CONDUCT FINISHED PRODUCT AND STABILITY TESTING UNDER CONTRACT FOR VARIOUS CLIENTS. THIS INSPECTION DID NOT RESULT IN THE ISSUANCE OF A FD 483. FOUR VERBAL OBSERVATIONS WERE DISCUSSED REGARDING CGMP ISSUES. MANAGEMENT INITIATED CORRECTIVE ACTION TO THESE OBSERVATIONS PRIOR TO THE CLOSE OF THE INSPECTION. BASED UPON THIS INSPECTION AND THE FIRM'S INSPECTION HISTORY, MIN-DO RECOMMENDS THEM AS ACCEPTABLE.				BASED ON FILE REVIEW	
OC RECOMMENDATION	06-JAN-2010			ACCEPTABLE DISTRICT RECOMMENDATION	INYARDA
SUBMITTED TO OC	30-JUL-2012				CUFFA
OC RECOMMENDATION	30-JUL-2012			ACCEPTABLE BASED ON PROFILE	SAFAAIJAZIR

Reference ID: 3244056

Chemistry Assessment Section

Establishment: CFN: (b) (4) FEI: (b) (4)
(b) (4)

DMF No: **AADA:** N 022110

Responsibilities: FINISHED DOSAGE STABILITY TESTER

Establishment Comment: MICROBIOLOGICAL TESTING OF STABILITY SAMPLES. (on 23-MAR-2009 by J. DAVID () 3017964247)

Profile: CONTROL TESTING LABORATORY **OAI Status:** NONE

Milestone Name / Comment	Milestone Date	Request Type	Planned Completion	Decision / Reason	Creator
SUBMITTED TO OC	23-MAR-2009				DAVIDJE
OC RECOMMENDATION	23-MAR-2009			ACCEPTABLE BASED ON PROFILE	FERGUSONS
SUBMITTED TO OC	23-DEC-2009				DAVIDJE
SUBMITTED TO DO	24-DEC-2009	Product Specific			INYARDA
ASSIGNED INSPECTION TO IB	29-DEC-2009	Product Specific			ESMITH1
INSPECTION SCHEDULED	(b) (4)				ESMITH1
INSPECTION PERFORMED					ESMITH1
INSPECTION PERFORMED See Endorsement Text.					MATTHEW.DIONNE
DO RECOMMENDATION	27-JAN-2010			ACCEPTABLE INSPECTION	ESMITH1
OC RECOMMENDATION	28-JAN-2010			ACCEPTABLE DISTRICT RECOMMENDATION	INYARDA
SUBMITTED TO OC	30-JUL-2012				CUFFA
SUBMITTED TO DO	30-JUL-2012	10-Day Letter			SAFAAIJAZIR
DO RECOMMENDATION PREVIOUS THREE EI DRUG INSPECTIONS (2012, 2010, AND 2008) WERE CLASSIFIED VAI AND NAI FOR PROFILE CLASS CTL. DISTRICT RECOMMENDS APPROVAL BASED ON COMPLIANCE HISTORY OF THE FIRM.	01-AUG-2012			ACCEPTABLE BASED ON FILE REVIEW	CLE
OC RECOMMENDATION	02-AUG-2012			ACCEPTABLE DISTRICT RECOMMENDATION	INYARDA

Chemistry Assessment Section

Establishment: **CFN:** (b) (4) **FEI:** (b) (4)
(b) (4)

DMF No: **AADA:** N 022110

Responsibilities: DRUG SUBSTANCE MANUFACTURER

Establishment Comment: DRUG SUBSTANCE IS AN NME. THIS FACILITY IS RESPONSIBLE FOR MANUFACTURING AND RELEASE TESTING. (on 23-MAR-2009 by J. DAVID () 3017964247)

Profile: (b) (4) **OAI Status:** NONE

Milestone Name / Comment	Milestone Date	Request Type	Planned Completion	Decision / Reason	Creator
SUBMITTED TO OC	23-MAR-2009				DAVIDJE
SUBMITTED TO DO	23-MAR-2009	Product Specific			STOCKM
DO RECOMMENDATION	06-APR-2009			ACCEPTABLE BASED ON FILE REVIEW	JOHNSONE
OC RECOMMENDATION	06-APR-2009			ACCEPTABLE DISTRICT RECOMMENDATION	STOCKM
SUBMITTED TO OC	23-DEC-2009				DAVIDJE
SUBMITTED TO DO	24-DEC-2009	Product Specific			INYARDA
DO RECOMMENDATION	19-JAN-2010			ACCEPTABLE BASED ON FILE REVIEW	JOHNSONE
OC RECOMMENDATION	19-JAN-2010			ACCEPTABLE DISTRICT RECOMMENDATION	STOCKM
SUBMITTED TO OC	30-JUL-2012				CUFFA
SUBMITTED TO DO	30-JUL-2012	10-Day Letter			SAFAAIJAZIR
UNDER REVIEW	31-JUL-2012				PHILPYE
DO RECOMMENDATION INSPECTION ENDING (b) (4) CLASSIFIED VAI.	27-AUG-2012			ACCEPTABLE BASED ON FILE REVIEW	STOCKM
OC RECOMMENDATION	31-AUG-2012			ACCEPTABLE DISTRICT RECOMMENDATION	SAFAAIJAZIR

####

Reference ID: 3244056

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

MARK R SEGGEL
01/11/2013

RAPTI D MADURAWE
01/11/2013

NDA 22-407

VIBATIV™

(telavancin hydrochloride)
For Injection

Theravance, Inc.

Balajee Shanmugam, Ph.D
Division of Pre-Marketing Assessment, Branch V
ONDQA

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Chemistry Review Data Sheet

1. NDA 22-407

2. REVIEW #: 2

3. REVIEW DATE: 1-NOV-2010

4. REVIEWER: Balajee Shanmugam, Ph.D.

5. PREVIOUS DOCUMENTS: NA

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Resubmission	30-June-2010

7. NAME & ADDRESS OF APPLICANT:

Name:	Theravance, Inc.
Address:	901 Gateway Boulevard, South San Francisco, CA 94080.
Representative:	Rebecca Coleman, PharmD
Telephone:	650-808-6076

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: VIBATIV™
b) Non-Proprietary Name (USAN): telavancin
c) Code Name/# (ONDC only):
d) Chem. Type/Submission Priority (ONDC only):

- Chem. Type: 3
- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505(b) (1)

10. PHARMACOL. CATEGORY: Antibacterial

11. DOSAGE FORM: Sterile lyophilized powder for injection

12. STRENGTH/POTENCY: 250 and 750 mg

13. ROUTE OF ADMINISTRATION: Intravenous infusion

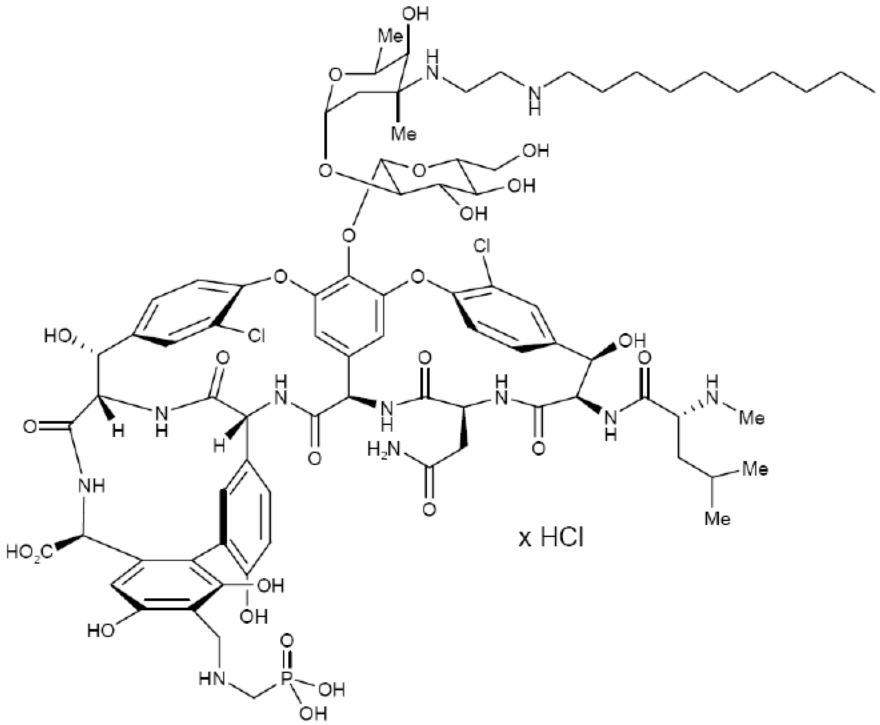
14. Rx/OTC DISPENSED: _X_Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
_____SPOTS product – Form Completed

___X__Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Vancomycin, N3″ [2 (decylamino) ethyl] 29 [[(phosphono-methyl) amino] methyl] hydrochloride.
Molecular formula: $C_{80}H_{106}Cl_2N_{11}O_{27}P$. xHCl (where x= 1-3)
Molecular weight: 1755.63 (free base)
CAS: 380636-75-9



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")
[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

The Chemistry Review for NDA 22-407

The Executive Summary

Recommendation and Conclusion on Approvability

Telavancin is a lipoglycopeptide antibiotic which in this application is indicated for the treatment of nosocomial pneumonia.

The company has cross referenced NDA 22-110 for CMC information which was previously reviewed by this reviewer and recommended Approval from Chemistry perspective. Please refer to Chemistry reviews of NDA 22-110 by this reviewer for further information.

NDA 22-407 was issued a Complete Response and the resubmission under review was submitted on 30-June-2010. There is no new CMC information in this submission. Office of Compliance had recommended Approval of the facilities on 10-Feb-2010. The EES summary report is provided below.

In accordance to 21 CFR 314.50, NDA 22-407 by way of cross-reference to NDA 22-110 provides adequate information on manufacturing and packaging procedures, in-process controls, methods, and specification. Therefore, from chemistry perspective, the application is recommended for Approval.

ESTABLISHMENT EVALUATION REQUEST SUMMARY REPORT

APPEARS THIS WAY ON ORIGINAL

Application:	NDA 22407/000	**Sponsor:**	THERAVAN
Org. Code:	520		901 GATEW
Priority:	1		SOUTH SAI
Stamp Date:	26-JAN-2009	**Brand Name:**	VIBATIV
PDUFA Date:	30-DEC-2010	**Estab. Name:**	
Action Goal:		**Generic Name:**	
District Goal:	24-DEC-2009	**Product Number; Dosage Form;**	
		001; POWDER, FOR INJECTI TELAVANCIN HYDROCHLOR	
		002; POWDER, FOR INJECTI TELAVANCIN HYDROCHLOR	

FDA Contacts:	J. DAVID	Project Manager
	B. SHANMUGAM	Review Chemist
	N. SCHMUFF	Team Leader

Overall Recommendation:	ACCEPTABLE	on 10-FEB-2010	by C. CRUZ
	ACCEPTABLE	on 22-JUN-2009	by FERGUSONS

Establishment:	**CFN:** (b) (4)	**FEI:** (b) (4)	
	(b) (4)		
DMF No:		**AADA:**	N 022110
Responsibilities:	FINISHED DOSAGE MANUFACTURER		
Profile:	SMALL VOLUME PARENTERAL, LYOPHILIZED	**OAI Status:**	NONE
Last Milestone:	OC RECOMMENDATION		
Milestone Date:	10-FEB-2010		
Decision:	ACCEPTABLE		
Reason:	DISTRICT RECOMMENDATION		

Establishment:	**CFN:** (b) (4)	**FEI:** (b) (4)	
	(b) (4)		
DMF No:		**AADA:**	N 022110
Responsibilities:	FINISHED DOSAGE STABILITY TESTER		
Profile:	CONTROL TESTING LABORATORY	**OAI Status:**	NONE
Last Milestone:	OC RECOMMENDATION		
Milestone Date:	06-JAN-2010		
Decision:	ACCEPTABLE		
Reason:	DISTRICT RECOMMENDATION		

Chemistry Assessment Section

Establishment:	CFN: (b) (4) FEI: (b) (4) (b) (4)		
DMF No:		AADA:	N 022110
Responsibilities:	FINISHED DOSAGE STABILITY TESTER		
Profile:	CONTROL TESTING LABORATORY	OAI Status:	NONE
Last Milestone:	OC RECOMMENDATION		
Milestone Date:	28-JAN-2010		
Decision:	ACCEPTABLE		
Reason:	DISTRICT RECOMMENDATION		

Establishment:	CFN: (b) (4) FEI: (b) (4) (b) (4)		
DMF No:		AADA:	N 022110
Responsibilities:	DRUG SUBSTANCE MANUFACTURER		
Profile:	(b) (4)	OAI Status:	NONE
Last Milestone:	OC RECOMMENDATION		
Milestone Date:	19-JAN-2010		
Decision:	ACCEPTABLE		
Reason:	DISTRICT RECOMMENDATION		

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

BALAJEE SHANMUGAM
12/01/2010
CMCReview2

STEPHEN P MILLER
12/03/2010
I concur - this NDA is recommended for approval from the CMC perspective.

NDA 22-407

VIBATIV™

(telavancin hydrochloride)
For Injection

Theravance, Inc.

Balajee Shanmugam, Ph.D
Division of Pre-Marketing Assessment, Branch IV
ONDQA

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Chemistry Review Data Sheet

1. NDA 22-407

2. REVIEW #: 1

3. REVIEW DATE: 14-SEPT-2009

4. REVIEWER: Balajee Shanmugam, Ph.D.

5. PREVIOUS DOCUMENTS: NA

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original submission	23-Jan-2009

7. NAME & ADDRESS OF APPLICANT:

Name:	Theravance, Inc.
Address:	901 Gateway Boulevard, South San Francisco, CA 94080.
Representative:	Rebecca Coleman, PharmD
Telephone:	650-808-6076

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: VIBATIV™
b) Non-Proprietary Name (USAN): telavancin
c) Code Name/# (ONDC only):
d) Chem. Type/Submission Priority (ONDC only):

- Chem. Type: 3
- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505(b) (1)

10. PHARMACOL. CATEGORY: Antibacterial

11. DOSAGE FORM: Sterile lyophilized powder for injection

12. STRENGTH/POTENCY: 250 and 750 mg

13. ROUTE OF ADMINISTRATION: Intravenous infusion

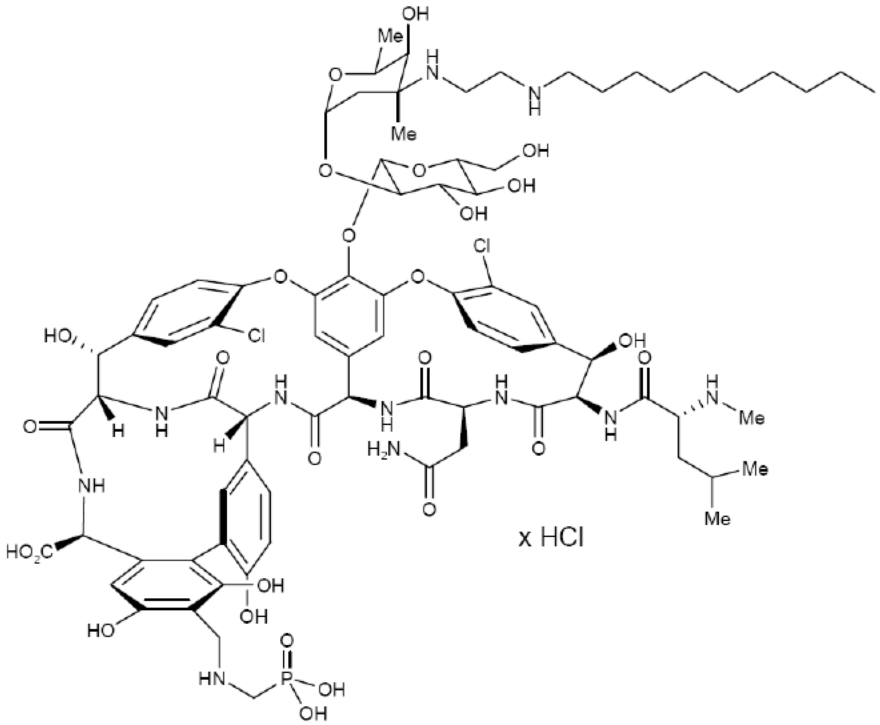
14. Rx/OTC DISPENSED: _X_Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
_____SPOTS product – Form Completed

___X__Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Vancomycin, N3″ [2 (decylamino) ethyl] 29 [[(phosphono-methyl) amino] methyl] hydrochloride.
Molecular formula: $C_{80}H_{106}Cl_2N_{11}O_{27}P$. xHCl (where x= 1-3)
Molecular weight: 1755.63 (free base)
CAS: 380636-75-9



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")
[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

The Chemistry Review for NDA 22-407

The Executive Summary

Recommendation and Conclusion on Approvability

Telavancin is a lipoglycopeptide antibiotic which in this application is indicated for the treatment of nosocomial pneumonia.

The company has cross referenced NDA 22-110 for CMC information which was previously reviewed by this reviewer and recommended Approval from Chemistry perspective. Please refer to Chemistry reviews of NDA 22-110 by this reviewer for further information.

In accordance to 21 CFR 314.50, NDA 22-407 by way of cross-reference to NDA 22-110 provides adequate information on manufacturing and packaging procedures, in-process controls, methods, and specification. Therefore, from chemistry perspective, the application is recommended for Approval.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22407	ORIG-1	THERAVANCE INC	VIBATIV

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

BALAJEE SHANMUGAM
09/29/2009
CMC Review

STEPHEN P MILLER
09/30/2009
I concur, as Acting Branch Chief